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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,098	12/05/2003	Klaus Bosslet	DORRIE-0007	7295

23599 7590 03/16/2007
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EXAMINER

PESELEV, ELLI

ART UNIT	PAPER NUMBER
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1623

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/728,098

Applicant(s)

BOSSLET ET AL.

Examiner

Elli Peselev

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12 and 23-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12 and 23-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The terminology "m is 3 to 5" is not disclosed in the specification as originally filed.

Claims 1-10, 12 and 23-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) Breadth of the Claims.

The claims encompass an immense number of species. Note that the number of variables in claim 1 exceeds 100.

(B) The predictability or lack thereof in the art.

Relative minor changes in epothilone compounds can convert a drug that is active cytotoxic agent to a drug that is inactive. Note, for example, that Nicolaou et al (U.S. Patent No. 6,441,186) disclose in Example 5, column 46 that while oxazole

analogs had cytotoxic activity comparable to thiazole analogs, the 4,4-ethano-epothilones proved inactive. Nicolau et al further state that "These results underscore the importance of conformational precision in these compounds for biological activity".

(C) The presence or absence of working examples.

No working examples showing an activity for any of the claimed compounds have been presented.

(D) The quantity of experimentation needed.

Because there is no way to predict a priori which compounds will be active from the specification or chemical structures alone, an extraordinary amount of trial and error experimentation is required to identify the active compounds.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Applicant contends that the objective evidence of record and known to one of ordinary skill in the art, including Nicolau but considered with the other evidence already of record (U.S. Patent Nos. 6,982,276 and 7,008,936) is, in fact contrary to shedding doubt on the inventors' statement. This argument has not been found persuasive. The disclosure in the U.S. Patent No. 6,982,276 is limited to epothilone analogs substituted by 1-methyl-2-(2-methyl-4-thiazolyl)ethenyl. Further, U.S. Patent No. 7,008,936 discloses treating cancer with the same compound as disclosed by U.S. Patent 6,982,276. The present claims are directed to a vast number of conjugates having structural formulas very different from the prior art compounds. For example, the claimed compounds wherein L1, L2 and L3 are linker-recognition unit of formula III are

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not structurally analogous to the prior art compounds. Therefore, there is a good reason to doubt that the claimed compounds would have the same or similar activity as structurally different prior art compounds.

The declaration submitted by applicant has been considered but has not been found persuasive because none of the compounds tested in the declaration is within the scope of the claimed compounds i.e. none of the tested compounds is directed to the claimed conjugate having the linker-recognition unit of formula (III).

Further, there is no evidence in the prior art cited that epithilone compounds are effective in the treatment of inflammatory diseases, neurodegenerative diseases, angiogenesis-associated diseases, multiple sclerosis, Alzheimer's disease and rheumatoid arthritis as set forth in claim 25.

Drug discovery is one of the most labor intensive and expensive types of inventions; it can cost over \$500 million to bring a single new drug to market. The specification fails to provide any evidence of any activity for the claimed compounds. Since the claimed compounds have significant structural differences from the prior art compounds, it cannot be predicted if the claimed compounds will have activity which is comparable to the activity of the prior art compounds.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elli Peselev whose telephone number is (571) 272-0659. The examiner can normally be reached on 8.00-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elli Peselev


ELLI PESELEV
PRIMARY EXAMINER
GROUP 1200